

JAN 05 2004

OFFICIAL



UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. Box 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

Fax Cover Sheet

Date: 05 Jan 2004

To: Donna M. Ferber	From: Malgorzata A. Walicka
Application/Control Number: 09/724,296	Art Unit: 1652
Fax No.: (703) 872-9307	Phone No.: (703) 305-7270
Voice No.: (303) 499-8080	Return Fax No.: (703) 305-3014
Title:	CC:
<input checked="" type="checkbox"/> Urgent <input type="checkbox"/> For Review <input type="checkbox"/> For Comment <input type="checkbox"/> For Reply <input type="checkbox"/> Per Your Request	

Comments:

Dear Ms. Ferber:

Please find enclosed the copy of the last Office Action in the above captioned case.

Sincerely

M. A. Walicka

Number of pages 7 including this page

STATEMENT OF CONFIDENTIALITY

This facsimile transmission is an Official U.S. Government document which may contain information which is privileged and confidential. It is intended only for use of the recipient named above. If you are not the intended recipient, any dissemination, distribution or copying of this document is strictly prohibited. If this document is received in error, you are requested to immediately notify the sender at the above indicated telephone number and return the entire document in an envelope addressed to:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BEST AVAILABLE COPY

Office Action Summary	Application No. 09/724,296		Applicant(s) DOETSCH ET AL.	
	Examiner Malgorzata A. Walicka		Art Unit 1652	
	The MAILING DATE of this communication appears on the cover sheet with the correspondence address --			

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on 09 October 2003.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 21-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 21-25 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)

3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☒ Other: Copy of paper by Kanno et al..

Application/Control Number: 09/724,296

Page 2

Ar. Init: 1652

The Amendment under 37 C.F.R. 1.111 filed on October 9, 2003 is acknowledged. Claims 21-23 and 25 are amended. Claims 21-25 are pending in the application and are the subject of this Office Action.

Office Action

1. Objections

A claim 21 is objected to because of the typographical error. Line 8 contains two articles "an a".

2. Rejections

2.1. 35 USC section 102

Rejection withdrawals

Rejection of Claim 25 under 35 U.S.C. 102(b) as being anticipated by Yajima et al. (The EMBO Journal 1995, 14, 2393-2399) made in the previous Office Action is withdrawn, because the Applicants arguments are found persuasive. Yajima et al.'s enzyme and assay have not been applied to DNA lesions recited by claim 25.

Rejection of claim 25 under 35 U.S.C. 102(b) as being anticipated by PCT Publication WO 99/04626 (WO) issued on February 4 1999; inventor/applicant Ballacosa A. et al. is withdrawn because the claim has been amended by addition of a provision.

Rejection of Claims 21, 22 and 24 under 35 U.S.C. 102(b) as being anticipated by Takao et al. (Nucleic Acid Res. 1996, 24, 1267-1271) is withdrawn because the

BEST AVAILABLE COPY

Application/Control Number: 09/724,296

Page 3

Art Unit: 1652

claims have been amended and the method uses the enzyme that is at least 90% purified, whereas the prior art teaches the method wherein the enzyme was only 35% pure.

Examiner's response to the Applicants traverse

Although the rejection is withdrawn the examiner addresses below the traverse of the 102 rejection made in the current Remarks, page 4, line 18:

"The cited reference [Takao et al.'95] does not teach a truncated Uvlp protein which exhibits stability and high enzymatic activity in a substantially purified state."

Applicants' argument has been fully considered, but is found not persuasive. Takao et al. cloned the gene of *S. pombe* UVDE endonuclease of which amino acids 239-599 are identical to SEQ ID NO: 4 of the instant application. Takao et al. showed that the enzyme is specific for pyrimidine dimers and 6-4 photoproducts. Takao et al. also demonstrated that truncation of the endonuclease up to 232 amino acid from the N-terminus does not influence the endolytic activity of the enzyme on UV irradiated DNA. Takao et al. expressed the protein consisting of amino acid 230-599 in *E. coli* and further used the truncated protein for incision of the UV irradiated DNA. Takao et al. experienced difficulties with purification of the yeast protein expressed in *E. coli*, whereas Applicants, who used as a host *S. cerevisiae* and expression of the truncated UVDE gene in frame with a glutathione-S-transferase leader sequence, a method routinely used in biotechnology for the expression and purification of a stable protein,

Application/Control Number: 09/724,296

Page 4

Art Unit: 1652

were successful in purification of the expressed protein to apparent electrophoretic homogeneity.

In conclusion, Takao et al. used the same method and the same enzyme as claimed in claims 21, 22 and 24 of the instant application. Takao et al. produce the enzyme in *E. coli* host cell comprising the gene encoding full enzyme or truncated enzyme consisting of amino acids 230-599. Although Takao et al. used in the same method the enzyme that was not 100% pure its endonucleolytic activity was directed to the UV irradiated DNA containing CPD and 6-4 PP. **The fact is that the enzyme (product) and the method of use of said product to the UV irradiated DNA containing photoproducts were taught by Takao et al. two years before Applicants** filed, on June 8, 1998, the provisional application No. 60/088521, of which the instant application claims benefit.

It is also worth mentioning in this context that Freyer G. A. et al. (An alternative eucaryotic DNA excision repair pathway, *Mol. Cell. Biol.* 1995, 15, 4572-4577), used crude extracts of *S. pombe* UVDE, whose amino acid sequence was unknown at that time, for incision *in vitro* of double stranded DNA containing cyclobutane pyrimidine dimers and 6-4 pyrimidine pyrimidones. Thus, the enzyme exhibits its activity in crude extracts, i.e., not purified. Therefore the purification is not a characteristic pertinent to specific activity.

Applicants in their Remarks, page 4 line 15 write, "Importantly, and surprisingly, the truncated Uvelp proteins [protein] or Uvelp

Application/Control Number: 09/724,296

Page 5

Art Unit: 1652

fusion proteins of the present invention are stable upon purification and retain enzymatic activity when substantially purified."

This argument is not found persuasive, as the claim is not directed to a method of applying the truncated enzyme purified by a novel method. The expression of a protein of interest in frame with GST and the subsequent purification on glutathione containing column, plus/minus cleavage GST with trombin is used in biotechnology routinely for production of large quantities of enzymes that are stable after this purification.

Further, on page 5, Applicants argue, "Moreover, the cited reference [Takao] does not teach endonuclease activity on all the types of distorted DNA as taught in the present case."

Indeed, that is why the examiner does not reject the use of truncated *S. pombe* UVDE according to its novel activities disclosed by Applicants. **The novel endolytic activities are directed towards following lesions: Dewar isomer of 6-4 photoproduct, apurinic site, uracil, dihydrouracil (not recited by the claims), platinum-DNA GG diadduct, mismatched nucleotide, and loop of less than 5 nucleotides.**

2. 35 USC section 103

Claims 21- 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Takao et al. (Nucleic Acid Res. 1996, 24, 1267-1271) in view of Ford et al. (Fusion Tails for

Application/Control Number: 09/724,296

Page 6

Art Unit: 1652

the Recovery and Purification of Recombinant Proteins, Protein expression and purification, 1991, 2, 95-107.

Claims 21-22 and 24 are directed to the method for cleavage of a double-stranded DNA molecule containing a distorted structure wherein the distortion is caused by UV irradiation, a photoproduct, when the cleavage enzyme is set forth by SEQ ID NO: 4 consisting of truncated *S. pombe* UVDE endonuclease amino acids residues 230-823 and when the enzyme is at least 90% pure.

Claim 23 is directed to the method for cleavage of a double-stranded DNA molecule containing a distorted structure wherein the distortion is caused by UV irradiation, a photoproduct, when the cleavage enzyme is set forth by SEQ ID NO: 6 consisting of glutathione-S-transferase leader followed by amino acids residues 230-828 of *S. pombe* UVDE endonuclease, i.e. a fusion of GST and truncated sequence and *S. pombe* UVDE endonuclease.

Takao et al. cloned *S. pombe* UVDE endonuclease gene consisting of 599 amino acids, identical to amino acids 230-828 of SEQ ID NO: 2 of the instant application. Takao et al. teach the method of incision of double stranded DNA distorted by irradiation with UV, containing 6-4 photoproduct and cyclobutane pyrimidine dimers, using their UVDE endonuclease, page 1268, left column; see subtitles *Plasmid nicking assay* and *Incision assay using synthetic oligonucleotides*. Takao et al. expressed the enzyme in *E. coli* and purified it using as the first step heparin-Sepharose column and subsequently blue-Sepharose, page 1269, left column, line 11. However, they experienced difficulties in purification of a stable protein from *E. coli*. Takao et al. also

Application/Control Number: 09/724,296

Page 7

Art Unit: 1652

reported successful expression of UVDE gene in *S. cerevisiae*; page 1271, right column, line 20.

Takao et al. do not teach, however, how to efficiently recover and purify the UVDE enzyme expressed in any microorganism.

Ford et al. teach that making a fusion protein consisting of glutathione-S-transferase tail (GST) and an enzyme of interest, page 96, right column, line 29, enables efficient recovery and purification using the affinity column containing immobilized glutathione. The GST can be subsequently cleaved out of the enzyme by thrombin, if the fusion protein is not active.

It would have been obvious to one having ordinary skill in the art at the time of invention to have the method of DNA cleavage of Takao et al. and to modify the expression and purification of UVDE endonuclease as taught by Ford.

The motivation for the modification would be to have a large quantity of pure and stable enzyme necessary for the method. The motivation is provided by Ford et al. who state, "On a lab scale, fusion tail recovery systems are powerful and elegant tools for one-step recovery and purification of recombinant proteins or identification of proteins encoded by cloned cDNAs. On an industrial scale, fusion tail technology can be used in the recovery and purification of both higher-cost pharmaceuticals and lower-to medium-cost enzymes."

The expectation of success in obtaining stable and pure truncated *S. pombe* UVDE is very high because of well-developed and routine use of the glutathione-S-

Application/Control Number: 09/724,296

Page 8

Art Unit: 1652

transferase fusion protein, which may be used with (SEQ ID NO: 4) or without cleavage (SEQ ID NO: 6) of the GST leader by trypsin.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made, and was as a whole *prima facie* obvious.

Response to Applicants' traverse

In their Remarks, page 9, line 12, Applicants traverse this rejection stating, "There is nothing that suggests that this approach, specifically the GST approach, would allow the purification of a truncated UVDE that is stable."

Applicants' argument has been fully considered, but is found not persuasive. Firstly, Takao et al.'s problem with purification of the *S. pombe* UVDE was related to the full length as well as truncated form of the enzyme, so the question was not to obtain a truncated UVDE that is stable, but a stable and purified *S. pombe* UVDE. The GST approach that was used in the instant application is the most popular way of expressing and purifying proteins of interest. Other approaches using heterologous protein different from GST are also very efficient in obtaining a stable *S. pombe* UVDE. See, for example, Kanno et al. (Repair of apurinic/apirimidinic sites by UV damage endonuclease; a repair protein for UV and oxidative damage, Nucleic Acid Research, 1999, 27, 3096-3103). Kanno et al. expressed *S. pombe* UVDE in *E. coli* as a recombinant protein containing maltose-binding protein. This enzyme was then purified

Application/Control Number: 09/724,296

Page 9

Art Unit: 1652

on amylose column; see "Materials and Methods", subtitle Enzymes and Chemicals:
copy enclosed.

2. 35 USC, section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2.3.1. Lack of written description- new rejection

Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to the method for cleavage of a double stranded DNA molecule containing a platinum diadduct, intercalated molecule or alkylation of a nucleotide, wherein the cleaving enzyme is truncated *S. pombe* UVDE. The claims are directed to a genus of methods of cleaving double stranded DNA containing a genus of DNA lesions comprising the following subgenera:

- 3. a platinum diadduct,
- 4. an intercalating molecule, and

Application/Control Number: 09/724,296

Page 10

Art Unit: 1652

c) alkylation of a nucleotide.

Neither the subgenera of lesions nor the specific activity of the *S. pombe* truncated UVDE directed to these subgenera of lesions are sufficiently described.

The disclosure teaches that the truncated *S. pombe* UVDE endonuclease is specific towards one form of platinum diadduct, platinum-DNA GG diadduct, however, the specification fails to teach that the enzyme is active towards other platinum-DNA diadducts.

The disclosure is silent as to any intercalating molecule, which, when intercalated into the double stranded DNA, is recognized by the truncated *S. pombe* UVDE endonuclease. This is a complete lack of written description.

The disclosure is silent as to any alkylation of a nucleotide which is recognized by the truncated *S. pombe* UVDE endonuclease. This is a complete lack of written description.

Given the lack of disclosure of activities of truncated *S. pombe* UVDE towards certain lesions as stated above, Applicants have failed to sufficiently describe the invention of claim 21-24 in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention when the application was filed.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Application/Control Number: 09/724,296

Page 11

Art Unit: 1652

The claim is directed to a genus of methods for cleavage of a double stranded DNA molecule containing lesions wherein the cleaving enzymes are set forth by SEQ ID NO: 36 (*Neurospora crassa* UVDE), SEQ ID NO: 37 (*Bacillus subtilis* homolog of UVDE), SEQ ID NO: 38 (*Homo sapiens* MED1 endonuclease specific for repair of the mismatched nucleotides) and SEQ ID NO: 39 (*Deinococcus radiodurans* homolog of UVDE). The claim is directed to a genus of methods of cleaving double stranded DNA containing a genus of DNA lesions comprising the following subgenera:

- a) an abasic site,
- b) mismatched nucleotide pairing,
- c) a platinum diadduct,
- d) an insertion deletion loop,
- e) alkylation of a nucleotide, and
- f) the presence of uracil residue,

with the proviso that when the endonuclease comprises the amino acid sequence of SEQ ID NO: 38, the distorted structure does not result from mismatched nucleotides.

The specification fails to teach that the polypeptides set forth by SEQ ID NOs: 36-39 have endonucleolytic activity directed to the lesions a) - f) above. The disclosure teaches the specificity of *S. pombe* UVDE, or its truncated form, towards an abasic site, mismatched nucleotide, platinum-DNA GG diadduct, an insertion deletion loop of less than 5 nucleotides, uracil and diuracil. Thus, claim 25 suffers from a complete lack of written description regarding the claimed specificities of polypeptides of SEQ ID NO: 36-39. The examiner emphasizes that this is not the lack of enablement,

Application/Control Number: 09/724,296

Page 12

Art Unit: 1652

because one skilled in the art, using the guidance given by the specification, could determine whether polypeptides of SEQ ID NO: 36-39 have the endolytic activities directed to lesion listed under a) -- d) and f).

In addition, the proviso "when the endonuclease comprises the amino acid sequence of SEQ ID NO: 38, the distorted structure does not result from mismatched nucleotides" is a new matter. No such provision was made in the specification and claims as originally filed.

Furthermore, the disclosure teaches how to measure specificity toward only one, and not any, platinum diadduct, i.e., towards platinum-DNA GG diadduct. The specification does not teach and does not provide evidence that any of the enzymes of SEQ ID NOs:36-39 have the activity towards any alkylated nucleotide, thus the claim is completely lacking written description.

Given the lack of disclosure activities of the enzymes towards certain lesions as stated above, Applicants have failed to sufficiently describe the invention of claim 25 in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention when the application was filed.

3.3.2. Lack of enablement -- new rejection

Claim 21-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Application/Control Number: 09/724,296

Page 13

Art Unit: 1652

The claims are directed to the method for cleavage of a double – stranded DNA molecule containing any alkylation of a nucleotide or/and to the method for cleavage of double-stranded DNA molecule containing any intercalated molecule. The specification, however, fails to teach any DNA lesion which is an alkylation of a nucleotide or any DNA lesion which is caused by intercalation of any DNA intercalating molecule. For that reason, the specification fails to teach that any of the enzymes, SEQ ID NOs: 4, 6, and 38-39 has an activity toward said lesions. Therefore, to make and use the claimed invention undue experimentation is necessary.

Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses a genus of methods for cleavage a damaged DNA molecule by six enzymes, when the scope of the chemical lesions encompasses any alkylation of a nucleotide out of large number of known and thus far unidentified alkylations, as well as any lesion caused by intercalation of any out of a large number of known and unidentified intercalating molecules. The art of the determination of the endolytic activities of repair enzymes is well developed and skills of artisans high. However, while enablement is not precluded

Application/Control Number: 09/724,296

Page 14

Art Unit: 1652

by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the methods used the claimed endonucleolytic activities. The unpredictability of specificity of polypeptides of SEQ ID NO: 4, 6, and 36-39 towards a specific alkylation or intercalation is high, thus the experimentation left to those skilled in the art has a low probability of success absent the detailed guidance regarding the structure of alkylation and intercalation.

The disclosure fails to provide such guidance regarding which of alkylated nucleotides and intercalations of which intercalating molecules are to be used as the substrates-lesions for repair enzymes of SEQ ID NO: 4, 6, and 36-39. Without a further guidance on the part of Applicants with regards to the structure of the generic lesions recited by the claims one skilled in the art is forced to improperly extensive and undue experimentation.

Conclusion

No claim is in conditions for allowance, however the claims contain the allowable subject matter. The following is the examiner reason for allowable subject matter.

Applicants disclose novel activities of the truncated form of the *S. pombe* endonuclease of SEQ ID NOs: 4 and 6. Said activities are used in the method of cleavage a double-stranded DNA containing the following lesions: **Dewar isomer of 6-4 photoproduct, abasic site, uracil, dihydrouracil (not recited by the claims),**

Application/Control Number: 09/724,296

Page 15

Art Unit: 1652

platinum-DNA GG diadduct, mismatched nucleotide, and loop of less than 5 nucleotides.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

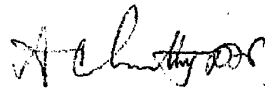
If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner


PONNATHAPUACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice of References Cited	Application/Control No. 09/724,296	Applicant(s)/Patent Under Reexamination DOETSCH ET AL.	
	Examiner Malgorzata A. Walicka	Art Unit 1652	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US			
	B	US			
	C	US			
	D	US			
	E	US			
	F	US			
	G	US			
	H	US			
	I	US			
	J	US			
	K	US			
	L	US			
	M	US			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	anno et al. Repair of apurinic/apirimidinic sites by UV damage endonuclease; a repair protein for UV and oxidative damage, Nucleic Acid Research, 1999, 27, 3096-3103.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
 Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

U.S. Patent and Trademark Office
 PTO-892 (Rev. 01-2001)

Notice of References Cited

Part of Paper No. 20031229